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10/527,588	06/07/2006	Federico Bussolino	WEICKM-0043	1009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,588	BUSSOLINO ET AL.	
	Examiner	Art Unit	
	Aaron J. Kosar	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election **with traverse** of Group I, claims 11-16 in the reply filed on July 30, 2007 is acknowledged. The traversal is on the ground(s) that burden has not been established and the reference of O'Brien does not render the invention obvious. This is not found persuasive because lack of unity of invention has been argued by the lack of a corresponding special technical feature among the claims and because O'Brien, to the extent the claims read upon a method of identifying and a composition comprising a HIV-1 TAT protein:HIV-1 gp120 inhibitor, for the reasons of record and those taught by O'Brien teaches a compound which inhibits viral entry by inhibiting the HIV-1 TAT:gp120 interaction. Thus the technical feature cannot be a contribution over the prior art and thus cannot be a *special technical feature*.

The election/restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1-22 are pending. Claims 1-10 and 17-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 30, 2007.

Claims 11-16 have been examined on the merits.

Information Disclosure Statement

The information disclosure statement filed March 14, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

The listing of references in the Search Report which are listed in the information disclosure statement (IDS) of March 14, 2005 does not comply with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed.

Therefore, the references cited in the International Search Report (ISR) and/or IDS which have not been provided to the Office according to 37 CFR 1.98, have not been considered and have been marked by a line-through of the reference or strike-out of a block of references. The IDS has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 12 is objected to because of the following informalities: The phrase "is tested..sequential" appears to be a typographical error of the phrase are tested..sequentially". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 16 is rejected under 35 U.S.C. 101 because claim 11, steps (i)-(ii) claim a method of identifying (method of *making*) a compound which inhibits HIV-1 entry into a host cell, while

claim 16 claims a method of *using* the *compound* recited in claim 11 or compounds desired therefrom in a formulated pharmaceutical *composition*. The method of identifying/characterizing a compound concludes with the identification/characterization of the compound; thus a compound which is formulated or derived/inspired/desired therefrom does not further limit a method of identifying/characterizing, but rather is drawn to a second method which by the dependency upon claim 11 impermissibly is drawn to two statutory classes of invention (identifying and using).

The claim is rejected because the claims are drawn to two inventions (1st method of using to identify a compound vs. 2nd method of using the identified product of the 1st method to formulate a composition), each of which is a patentably distinct invention, within a single claim, although Applicant may only claim one statutory class of invention in a claim/series of dependent claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a *contacting step* in which the reaction of the sample with the reagents necessary for the assay is recited, a *detecting step* in which the reaction steps are quantified or visualized, and a *concluding/correlating step*

describing how the results of the assay allow for the determination. Please note, "determining" *per se* (see claim 11,step (ii)) may reasonably be interpreted as reciting a mental process which does not positively recite an active step and does not set forth the step by which one *determines* the *capability to inhibit* and thus the step of determining is not further limiting or descriptive of the method set forth in step (i). In these claims, the reagents are recited (step (i)); however, the remaining active steps are missing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by JAIN ((**U1**: PTO 892) Jain, K.K. "Evaluation of memantine for neuroprotection in dementia" Expert Opinion of Investigational Drugs. 2000, 9(6), 1397-1406.).

The claims are generally drawn to providing a compound. The dependent claims are further drawn to testing order; the number of compounds (plurality versus library); and the nature of the test (cellular- versus molecular-based).

JAIN teaches that "[HIV-1] Tat and gp120 proteins act synergistically to potentiate each other's neurotoxic effects". Jain teaches incubating Tat and gp120 (a molecular-based model) and *in vivo/in vitro* studies (cell-/organismal-based models). Jain also teaches that the neurotoxicity caused by the combination of Tat and gp120 "can be blocked completely by memantine, partially by amiloride, and not at all by dipyridamole or vagabatrin"(page 1401,

§5.1.4, ¶2). Although the reference may be silent with regard to the mechanism of host cell entry of HIV-1, to the extent Jain teaches (a) the plurality/library of *compounds/molecules* memantine and ameloride, (b) the binding of memantine to protein (42-45%, page 1401, §5.1.5), (c) the *interaction* of synergism between the HIV-1 proteins Tat and gp120, and (d) *inhibition* by complete/partial blockage of the effect of Tat and gp120 (page 1401), including effects upon cells, one may broadly and reasonably interpret the determinations of completely-, partially-, or non-blocked status as an *identification/ characterization method* of a compound which inhibits HIV-1 entry into a host cell (page 1401, §5.1.4, ¶2).

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by O'BRIEN (**U:** PTO-892 3/29/2007).

The teachings of the claims are above.

O'Brien teaches a compound, ALX40-4C, which is interacts with Tat and with gp120 . O'Brien also teaches that the compound has a core peptidic structure and a cationinc +9 charge which maps to a HIV-1's envelope protein. O'Brien also teaches that the "determinants for efficient ALX40-4C inhibition were mapped by using recombinant virus strains to the V3 region of gp120 and were shown to act at early events in viral replication which include viral entry" (abstract; pages 2827 and 2828). To the extent that inhibition of a gp120:Tat interaction may be measured as the "inhibition of entry of HIV-1 into a host cell" and in view of the effect that inhibiting the initial attachment of the HIV-1 gp120 to a cell has on downstream steps - equating to a net inhibition of HIV-1 entry because of a reduced binding probability – O'Brien may be broadly and reasonably be interpreted as teaching inhibition of gp120:Tat.

Claims 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by ESTE ((**X1**:PTO-892)Esté, José A., et al "Human Immunodeficiency Virus Glycoprotein gp120 as the Primary Target for the Antiviral Action of AR177 (Zintevir)" Molecular Pharmacology 1988, 53(2), 340-345.).

The teachings of the claims are above.

ESTE teaches a HIV-1 gp120 protein-targeting compound, AR177 (T30177, Zintevir). Este teaches a molecular-based assay in teaching an immobilized gp120 versus AR177 (page 341, left column, ¶5) and a cellular-based assay ("syncytium formation assay", page 341, right column, ¶ 5). Este also teaches a second tested compound/molecule, AZT, which is identified as not inhibiting the binding of HIV strains to CD-positive cells (page 343, right column, ¶3). Furthermore, the teaching of a plurality of HIV-1-treating compounds (AZT, AR177, AMD3100, DS, heparin, etc.), and testing in the manner taught by Este, teaches testing a library of chemical compounds.

Claims11-16 are rejected under 35 U.S.C. 102(a) as being anticipated by JAYASURIA ((**V1**:PTO-892) Jayasuria, H, et al. Journal of Natural Products. 2002, 65(8), 1091-1095.).

JAYASURIA teaches screening a library of microbial fermentation extracts to determine Tat protein inhibitors. Jayasuria teaches a plurality of compounds derived from the library, including durhamycin A, durhamycin B, compound (3), and the aglycone (4). Jayasuria also teaches the determination of the inhibition concentration (IC_{50}) of the compounds versus HIV-1 transactivation, including using cellular/molecular-based assays, including using 96-well plates (parallel reaction).

Claims 11-16 are rejected under 35 U.S.C. 102(a) as being anticipated by DECLERCQ ((**W1**:PTO-8920 De Clercq, E. "New Developments in anti-HIV chemotherapy" Biochim. Biophys. Acta. (2002) 1587(2-3), 258-275.).

The teachings of the claims are above.

DECLERCQ teaches a inhibitors of gp120 which adsorb/chelate/shield the gp120 domain of the viral envelope glycoprotein. De Clercq also teaches inhibition of gp120:cell surface binding by adsorption of an inhibitor to the gp120 domain (§2, pages 259-260). To the extent that inhibition of the gp120:Tat interaction may be measured as the "inhibition of entry of HIV-1 into a host cell" and in view of the effect that inhibiting the initial attachment of the HIV-1 to a cell has on downstream steps - equating to a net inhibition of HIV-1 entry because of a reduced binding probability – De Clercq may broadly and reasonably be interpreted as teaching inhibition of gp120:Taq.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAIN (**U1**) *or* O'BRIEN (**U**) *or* JAYASURIA (**V1**) *or* DECLERCQ (**W1**) *or* ESTE (**X1**) as applied to claims 11-16 above and for the reasons below.

The teachings of the claims are above.

To the extent the prior art may be silent with respect to explicitly reciting a particular sequence of steps, it would have been obvious to perform the processes in

parallel, sequentially, or in any order, because selection of any order of performing process steps is *prima facie* obvious especially in the absence of new or unexpected results (see, e.g., *Ex parte Rubin*, 128 USPQ 440, 1959, and *In re Burhans*, 154 F.2d 690, 69 USPQ 330 - CCPA 1946) MPEP § 2144.04.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aaron J. Kosar whose telephone number is (571) 270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Aaron Kosar
Examiner, Art Unit 1651

SANDRA E. SAUCIER
PRIMARY EXAMINER